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Bronchoscopic lung volume reduction using coil therapy: complications and management

Abstract

Nonsurgical approaches involving bronchoscopic lung volume reduction (BLVR) have been developed in the last decade. One of these, the BLVR coil procedure, is a treatment option for patients with homogeneous and heterogeneous end-stage emphysema and a forced expiratory volume in 1 second (FEV₁) of 15–45%. This treatment decreases hyperinflation and improves lung function, the quality of life, and exercise capacity. It is very important to prepare patients for treatment, premedications, anesthesia applications, intubation, post-procedure follow-up and treatments. Further, it has been observed that various complications can develop during and after the procedure. Generally, the observed and reported complications are chronic obstructive pulmonary disease (COPD) exacerbation, chest pain, mild bleeding, pneumonia, pneumothorax, and respiratory failure. Rarely, aspergillus cavitation (coil-related aspergilloma), bronchopleural fistula and penetration into the pleural space, bronchiectasis, coil-associated inflammatory response and opacities, and hiccups are observed. Common complications are usually mild or moderate, while the rare ones can be life-threatening (except hiccups), so early diagnosis and treatment are necessary. However, patients treated with BLVR have lower mortality rates than untreated patients with similar morbidity. Based on the findings of this review, we can estimate that premedication one day before and just before the procedure may reduce potential complications. Some medical centers apply and recommend 30-day macrolide treatment after the procedure. New generation supraglottic devices may be preferred to avoid complications due to endotracheal intubation. Moreover, further research is needed to identify risk factors, prevent potential complications, and a common consensus is required for routine preventive treatment.

Key words: bronchoscopic, lung volume reduction, coil, complication, management

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Introduction

Emphysema is a chronic lung disease that causes pulmonary parenchymal damage, hyperinflation, loss of elastic recoil, and progressive dyspnea [1]. In the last stage of emphysema, there is a marked decrease in exercise capacity and the quality of life, and a consequent restriction of daily activities. During this period, long-acting bronchodilators (β_2 -agonist and anti-muscarinic) and drugs (phosphodiesterase-4 inhibitors, methylxanthines, and mucolytic agents) are administered to reduce the severity of symptoms and frequency of exacerbations [2]. In addition, smoking cessation, education and self-management, nutritional support, and pulmonary physiotherapy are recommended from the early stages of the disease [2].

However, when respiratory failure develops after a few years, long-term oxygen therapy at home becomes necessary, and in cases of hypercapnia, non-invasive mechanical ventilation is added [3]. While medical treatment of emphysema does not impact long-term outcomes in clinical practice, invasive treatment can be administered to very few patients.

Lung transplantation is an option for patients with forced expiratory volume in 1 sec (FEV₁) < 15–20%, but it is often not feasible due to a lack of organ availability and the need for specially experienced hospital personnel and equipment [4]. Studies conducted over the last 10 years have reported that the removal of nonfunctional lung parenchyma by lung volume reduction surgery may increase pulmonary function and improve

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the quality of life in patients [5, 6]. The 2014 National Emphysema Therapy Examination Trial emphasized the importance of patient selection for this treatment owing to the high incidence of postoperative complications (pulmonary and non-pulmonary) and early mortality [6].

Therefore, nonsurgical approaches involving bronchoscopic lung volume reduction (BLVR) have been developed in the last decade. One of these, the BLVR coil procedure, is a treatment option for patients with homogeneous and heterogeneous end-stage emphysema and an FEV₁ of 15–45% [7, 8]. This treatment decreases hyperinflation and improves lung function, the quality of life, and exercise capacity. In a review covering the studies conducted in 2012–2018, BLVR coil therapy showed an increase in FEV₁ values (mean + 130 mL, 12.1%), a decrease in residual volume (RV) (mean -420 mL, 16.5%) and a rise in 6-minute walking test (mean + 47 m) [7]. However, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2020 guidelines limit BLVR interventions to patients with advanced emphysema refractory to optimized medical treatment [2]. Further, it has been observed that various complications can develop during and after the procedure [9].

To this end, the main objective of this review is to determine the incidence of complications associated with BLVR coil treatment, both during the procedure and the follow-up period; to analyze the possible risk factors; and to discuss potential treatment options.

Material and methods

Four international databases (Google Scholar, Web of Science, SCOPUS and PubMed) have been crawled using specified keywords to obtain appropriate articles: endoscopic or bronchoscopic, lung volume reduction, coil, complication, and case reports. The “Related articles” section in Google Scholar and PubMed was used to obtain related and similar papers. Original articles, case reports, and case series were included.

Features of the BLVR coil procedure

Preparation of patients for the procedure

Patient preparation is very important prior to BLVR coil treatment (Table 1). Before the procedure, patients must have quit smoking, received pulmonary physiotherapy for at least 6 months, and be under optimal medical treatment. Pre-procedure arterial oxygen partial pressure and carbon dioxide partial pressure must be > 50 mm Hg and

Table 1. Preparation of patients

1. Determination of target lobe by HRCT and perfusion scintigraphy
2. Ensuring optimum inhaler treatment
3. Pulmonary physiotherapy (at least 6 months)
4. Smoking cessation (at least 4–6 months in advance)
5. Recommend pneumococcal and influenza vaccines
6. Evaluation of sPAP by echocardiography
7. Arterial blood gas analysis
8. Evaluation of the use of anticoagulants
9. Sputum culture
10. Prophylactic treatment: antibiotic, corticosteroid, nebulizer

HRCT — high resolution computed tomography; sPAP — systolic pulmonary artery pressure

< 55 mm Hg, respectively [9, 10]. It is essential to evaluate right ventricular function using transthoracic echocardiography prior to the BLVR procedure. Systolic pulmonary artery pressure > 50 mm Hg is considered a contraindication for BLVR coil therapy. The use of anticoagulants should also be considered as the BLVR coil procedure is contraindicated for patients on continuous treatment with anticoagulants, although there is no clear contraindication for those taking acetylsalicylic acid.

Premedication

Chronic obstructive pulmonary disease (COPD) exacerbation and pneumonia are the most common complications after the BLVR procedure [7]. In addition, acute inflammatory response to the procedure, and “coil-associated pneumonitis” have also been reported. Hence, many clinicians start corticosteroid (prednisolone 30 mg) and antibiotic (azithromycin 250 mg) prophylaxis in the preoperative period (1 day before) [10]. Corticosteroid treatment for 5 days and antibiotic therapy for 30 days after the procedure is recommended [10]. Despite insufficient supporting evidence in the literature, some BLVR treatment centers prefer β -lactam or macrolide use for 5–7 days postoperatively. In addition, some centers administer theophylline 200 mg, prednisolone 40 mg, levofloxacin 500 mg, and salbutamol/ipratropium nebulization 1 hour before BLVR [11].

Indication and protocol

The procedure is performed in patients with emphysema diagnosed by computed tomography who exhibit hyperinflated pulmonary functions [FEV₁: 15–45%, total lung capacity (TLC) > 100%, RV > 200%, and RV/TLC > 58%] [7, 9, 10]. Patients diagnosed with any other airway disease are not treated using this procedure. All coil implantations are performed using fi-

beroptic video bronchoscopy and fluoroscopic guidance. Ten standard (8–14 intervals) coils are implanted for each lung, and the second procedure is performed within 4–8 weeks. Patients without any complications are followed up in the hospital for an average of 1 day.

Anesthesia and intubation

Bronchoscopic lung volume reduction coil treatments are performed worldwide under general anesthesia. Generally, intubation with a 9-mm endotracheal tube and pressure-controlled ventilation at an inspiratory:expiratory ratio of 1:4 and respiratory frequency 10/min are preferred [10]. One study demonstrated I-gel supraglottic devices (SGD) (Intersurgical Ltd, Berkshire, UK) to be a safe alternative to endotracheal intubation in BLVR coil treatments [11]. I-gel SGD causes less bronchospasms, less mucosal/local trauma, and fewer hematomas than rigid bronchoscopy and endotracheal intubation, and the incidence of arytenoid dislocation is very low [12]. The size 8.5 of an endotracheal tube has a 57-mm cross-sectional area, while the new generation SGDs have a cross-sectional area of 127 mm [13]. This is very advantageous in that it makes the procedure easier and the complications of endotracheal intubation can be avoided.

Complications of endobronchial coil treatment

The complications of BLVR coil treatment can be divided into three groups based on when they occur: during the procedure, in the treatment

recovery (TR) period (< 30 days), and within the follow-up phase (> 31 days). Complications in the TR and follow-up periods are summarized in Tables 2 and 3, respectively.

During the procedure

Previous work has documented procedure-related complications which include mild bleeding (13.3%), coil repositioning and lengthening of the procedure (10%), and termination of the procedure due to deterioration in hemodynamic parameters (2.0%) [14]. In the same study, 31.6% of patients had to undergo aspiration of bronchial secretion and 8.1% of them showed *Pseudomonas aeruginosa* colonization, the significance of which is not yet clear. In addition, bronchospasm, headache, hoarseness, paroxysmal atrial fibrillation, and phlebitis may develop due to anesthesia after BLVR coil treatment [15].

In the treatment recovery and follow-up periods

Various complications can be seen during the periods following the BLVR procedure. These include bleeding, chest pain, COPD exacerbation, pneumonia, pneumothorax, and respiratory failure. Treatment recommendations for these complications are given in Table 4.

Bleeding

The most common complication observed during the TR period is mild bleeding or hemoptysis. Studies report the observation of this compli-

Table 2. An overview of treatment recovery period (0 to 30 days) complications in principal studies

| Author/study | Year | N | Baseline FEV ₁ [L] | Baseline FEV ₁ [%] | Hemoptysis | COPD exc. | Chest pain | Pneumonia | Pnx | Death |
|-----------------------------|------|-----|----------------------------------|----------------------------------|------------|--------------|---------------|-----------|------|-------|
| Slebos <i>et al.</i> [15] | 2012 | 16 | 0.72 ± 0.16 | 28.7 ± 7.1 | 75.0 | 21.4 | 14.2 | 7.1 | 3.5 | 0.0 |
| RESET study [16] | 2013 | 23 | 0.72 ± 0.17 | 27.1 ± 8.0 | 0.0 | 5.0 | — | 5.0 | 5.0 | 0.0 |
| Klooster <i>et al.</i> [17] | 2014 | 10 | 0.58 | 22.0 | 25.0 | 15.0 | 30.0 | 0.0 | 5.0 | 0.0 |
| Deslee <i>et al.</i> [18] | 2014 | 60 | 0.83 ± 0.25 | 30.1 ± 6.3 | 53.9 | 13.0 | 24.3 | 9.5 | 3.4 | 0.0 |
| Hartman <i>et al.</i> [19] | 2014 | 38 | — | 27.0 | 74.0 | — | — | — | 5.2 | — |
| Zoumot <i>et al.</i> [20] | 2015 | 45 | 0.76 ± 0.20 | 28.3 ± 8.0 | 0.0 | 4.8 | 1.2 | 1.2 | 6.0 | 0.0 |
| REVOLENS [21] | 2016 | 50 | 0.75 ± 0.25 | 25.7 ± 7.5 | 2.0 | 8.0 | 2.0 | 10.0 | 6.0 | 2.0 |
| RENEW [22] | 2016 | 158 | 0.71 ± 0.20 | 25.7 ± 6.3 | — | — | — | — | — | — |
| Gülser <i>et al.</i> [14] | 2017 | 40 | 0.68 ± 0.22 | 26.3 ± 9.1 | 10.0 | — | 25.0 | — | — | 0.0 |
| Kontogianni [23] | 2017 | 86 | 0.71 ± 0.21 | 27.7 ± 7.0 | 22.0* | 18.5* | 5.2* | 28.1* | 6.1* | 3.5* |
| Simon <i>et al.</i> [24] | 2018 | 33 | 0.46 ± 0.12 | 15.0 ± 3.0 | — | — | — | — | — | — |

*Adverse events within 3 months.

Data are shown as percentage. Events per procedure [14–18, 20, 21], events per patients [19, 23]

COPD — chronic obstructive pulmonary disease; exc. — exacerbation; FEV₁ — forced expiratory volume in 1 second; n — patients; pnx — pneumothorax

Table 3. An overview of follow-up (after > 31 days) complications in principal studies

| Author/study | Year | COPD exc. | Pneumonia | Chest Pain | Hemoptysis | Pnx | Resp. failure | Death |
|-----------------------------|------|-----------|-----------|------------|------------|-------|---------------|-------|
| Slebos <i>et al.</i> [15] | 2012 | 50.0 | 10.7 | 7.1 | 0.0 | 0.0 | — | 0.0 |
| RESET study [16] | 2013 | 7.0 | 0.0 | — | 0.0 | 0.0 | 0.0 | 0.0 |
| Klooster <i>et al.</i> [17] | 2014 | 35.0 | 0.0 | — | 0.0 | 10.0 | 0.0 | 0.0 |
| Deslee <i>et al.</i> [18] | 2014 | 60.2 | 17.2 | 10.7 | 5.3 | 3.2 | 0.0 | 0.0 |
| Hartman <i>et al.</i> [19] | 2014 | 51.0 | 46.0 | — | 0.0 | 6.0 | — | 3.0 |
| | | 37.0 | 7.0 | | 0.0 | 0.0 | | 8.0 |
| | | 36.0 | 5.0 | | 5.0 | 0.0 | | 6.0 |
| Zoumot <i>et al.</i> [20] | 2015 | 6.0 | 1.2 | 1.2 | 0.0 | 3.6 | — | 11.1 |
| REVOLENS [21] | 2016 | 24.0 | 12.0 | 2.0 | 0.0 | 2.0 | 2.0 | 6.0 |
| RENEW [22] | 2016 | 39.3* | 20.0* | — | 3.9* | 10.3* | 3.9* | 6.5* |
| Gülse <i>et al.</i> [14] | 2017 | 41.4 | 16.9 | 25.0 | 10.0 | 0.0 | — | 2.4 |
| Kontogianni [23] | 2017 | 12.3 | 7.9 | 0.0 | 3.5 | 1.7 | 2.6 | — |
| Simon <i>et al.</i> [24] | 2018 | 46.3** | 5.6** | 1.8** | 77.7** | 0.0** | 0.0** | 0.0** |

*Adverse events within 12 months; **Adverse events within 3 months.

Data are shown as percentage. Events per procedure [14–18, 20, 21]. Events per patients [19, 23].

COPD — chronic obstructive pulmonary disease; exc. — exacerbation; FEV1 — forced expiratory volume in 1 second; n — patients; pnx — pneumothorax

Table 4. Possible complications and suggestions [10, 11, 15–27, 30–36]

| Complication | Rates [%] | Suggestions |
|---|-----------|--|
| Aspergillus cavity | Rare | H, voriconazol |
| Bleeding, | | |
| Mild | 0–75.0 | M, interruption of acetylsalicylic acid treatment, |
| Severe | 1.5–3.5 | arterial embolisation or surgical intervention |
| Bronchopleural fistula | Rare | H, VATS or thoracoscopic removal of coil |
| Bronchiectasis | Rare | Only M, if patient remained asymptomatic |
| Chest pain | 0–25.0 | M, if persist removal of suspected coils near the pleura |
| Coil-associated inflammation and opacities | Rare | broad-spectrum antibiotics + systemic corticosteroid (0.5 mg/kg) |
| COPD exacerbation | 0–51.0 | H, ± systemic corticosteroid |
| Hiccup | Rare | M, if persist removal of suspected coils near diaphragma |
| Pneumonia | 0–46.0 | H, broad-spectrum antibiotics ± systemic corticosteroid |
| Pneumothorax | 0–10.3 | M, or inserting thorax tube |
| Respiratory failure | 0–3.9 | H, NIV or intubation |

COPD — chronic obstructive pulmonary disease; H — hospitalization; M — monitoring; NIV — non-invasive ventilation

cation in 0–75% of cases, whereas severe bleeding (> 150 mL) has rarely been noticed and appeared to resolve spontaneously in most cases [15–22]. Kontogianni *et al.* [23] reported severe bleeding in 3.5% of patients at the 1-year follow-up, and 3/4 of these patients required surgical intervention. In a study of bleeding complications, 65.3% of the subjects showing bleeding were in the TR period, and complications were more frequent in patients receiving acetylsalicylic acid treatment [24]. Bleeding improved spontaneously in 98.5%

of these patients, and persistent hemoptysis ameliorated after bronchial arterial embolization in 1.5% of the subjects [25]. Therefore, while anticoagulant use is contraindicated for this procedure, patients receiving acetylsalicylic acid therapy should also be treated with caution.

Chest pain

Chest pain or discomfort is common in the TR period and gradually diminishes during the

follow-up. If the chest pain is continuous and pleuritic, the coil implanted close to the pleura should be considered as the causative factor and assessed for removal. However, it can only be removed during the procedure and in the TR period [14]. A case of coil removal due to ongoing chest pain in the tenth month has been reported [26]. However, complete reversibility of the coils is not possible.

COPD exacerbations

The most common complication observed in the follow-up period is COPD exacerbation. Slebos *et al.* reported that COPD exacerbations were more frequent in the first month (here defined as “TR period”), and decreased in frequency subsequently [15]. Nevertheless, in a 3-year study, 51.0%, 37%, and 36% of COPD exacerbations were reported over the first, second, and third year, respectively [19]. It is thought that the frequent occurrence of COPD exacerbations in patients undergoing BLVR coil treatment is caused by local mucosal injury in the subsegmental airways, local edema, and the triggered secondary bronchoconstriction [15]. In the REVOLENS study, 2 g of amoxicillin/clavulanic acid (in the case of allergy, 600 mg of clindamycin plus 5 mg/kg of gentamicin) was recommended immediately before the BLVR procedure [21]. Although there is no clear consensus on preoperative preparation and therapy, we believe that this treatment regimen may be improved, and may reduce some complications, including exacerbation of COPD.

Pneumonia

The second most common complication in BLVR coil treatments is pneumonia or related pneumonitis. In the literature, the incidence of pneumonia is reported to be 14.8% on average (range 0.0–46.0%) [7]. Therefore, the benefits of using steroids and antibiotic regimens in cases of pneumonia (or pneumonitis) in the TR period should also be investigated in further studies.

Pneumothorax

Another potential complication after BLVR coil treatments is pneumothorax. It is observed in 3.4–6.1% of patients during the TR period [15–20, 23], and in 0.0–11.6% during the follow-up period [15–17, 19–24]. Pneumothorax is a serious complication that can cause respiratory failure, need for surgery, and even death. Patients who

develop pneumothorax must be hospitalized and monitored. Intercostal drainage or a thorax tube can be used if necessary [9]. Although there is an algorithm for predicting pneumothorax after BLVR valve treatment in the literature, there is no specific algorithm for pneumothorax after endobronchial coil treatment [27].

Respiratory failure

A possible complication of the BLVR procedure, respiratory failure was reported in 0.0–3.9% of patients after the TR period [16, 17, 21–24]. In contrast, in a meta-analysis conducted in 2015 involving 140 patients, respiratory failure was not reported [28]. These disparate results suggest the highly variable rates of respiratory failure, highlighting the need for further studies to evaluate contributing factors.

Rare and unexpected complications

There are some rare complications of BLVR coil treatments that may have serious consequences. These include *Aspergillus* cavitation (coil-related aspergilloma), bronchopleural fistula and penetration into the pleural space, bronchiectasis, coil-associated inflammatory response and opacities, and hiccups.

Aspergillus cavitation (coil-related aspergilloma)

Two case reports on this complication have been recently published [29, 30]. First case concerned the patient who underwent bilateral endobronchial coil treatment during the RENEW trial and developed a 27-mm cavity in the left upper lobe [29]. The patient was treated with voriconazole for 3 months and died due to decompensated respiratory failure. In the second case, the patient underwent endobronchial coil treatment for both upper lobes 3 years earlier [30]. Fungal cultures obtained during the procedure were positive for *Aspergillus* species, evaluated as colonization. *Aspergillus fumigatus* positivity was continued in the fungal cultures of the patient who continued spirometric improvement for the first 2 years. However, in the third year, computed tomography was performed because of worsening of dyspnea and frequent acute COPD exacerbations. Suspicious masses were observed in areas covering the distal end of the coils and the diagnosis was confirmed as aspergilloma. The patient was treated with voriconazole for about 14 months, and was discontinued due to cutane-

ous side effects. Aspergillus was not detected in ongoing cultures, clinical findings of the patient were stabilized and the follow-up continued. These two case reports highlight this rare complication, especially in the long term [29, 30].

Bronchopleural fistula and penetration into pleural space

This serious complication has been reported several times [23, 31–33]. This rare complication is due to the direct perforation of the bronchial wall and emphysematous tissue after coil implantation. It is usually observed in the first few days after the procedure. It may cause respiratory insufficiency, and in such cases, the coil should be removed thoracoscopically [34]. It is unclear whether this complication develops due to the proximity of the coils to the pleura; therefore, thoracic surgeons should be informed about the complication.

Bronchiectasis

Development of localized bronchiectasis a few months after endobronchial coil therapy has been reported in one case [35]. The cause of this complication and underlying mechanism are not yet known. The development of bronchiectasis may be an inflammatory response to a component of the coil or may be caused by tension in the subsegmental region, disrupting the blood supply to the bronchial artery and causing local ischemia [35]. In addition, the implantation of multiple coils into the same subsegment could have also led to this complication.

Coil-associated opacities and inflammatory response

Bronchoscopic lung volume reduction studies with lung sealant have revealed a new side effect of these treatments. This reaction is defined as the post-treatment acute inflammatory response [36, 37]. It usually includes chest pain or discomfort, cough, dyspnea, fever, negative microbiological findings, increased levels of inflammation markers (leukocytosis and high C-reactive protein levels), and low oxygen saturation. Similar findings have been found in cases of BLVR coil treatments. This phenomenon, described as coil-associated opacity (CAO), was first reported in 2016 in the RENEW trial [22]. The consolidations around the coils can mimic organized pneumonia and are usually non-infectious. Although the underlying mechanisms are not fully understood, it is generally accepted that this is a secondary inflammatory reaction due to

stress and traction force in the lung tissue, airway closure, local airway irritation, or local ischemia [10, 21, 22]. It is difficult to differentiate from bacterial pneumonia, and some patients may not have fever and excess sputum. Corticosteroid therapy (0.5 mg/kg) is recommended in addition to standard pneumonia treatment [10].

Interestingly, in other lung volume reduction procedures such as thermal vapor ablation, local inflammatory response is an indication of the efficacy of treatment [38]. Similarly, in patients who developed CAO after endobronchial coil treatment, there was a significant decrease in the volume of the targeted and treated lobe after complete recovery and resolution. These patients are thought to be the best responders [10, 39].

A report of two cases by Perch *et al.* showed a 34% improvement in basal FEV₁ in the patient who responded well to CAO treatment [40]. In the second subject, CAO was not included in the preliminary diagnoses and the patient died after circulatory collapse. Autopsy revealed necrotizing inflammation and organized pneumonia in the tissues around the coil. This demonstrates that CAO can lead to life-threatening consequences if not diagnosed and treated early. This suggests that patients may have an acute inflammatory reaction due to BLVR treatment, and inflammation markers must be closely monitored. The high values for inflammation markers have the potential to mask other infections that may develop, causing new infections to be missed. The duration for which these laboratory values continue to remain high and the extent to which they can be treated are separate research topics.

In a different report of two patients with severe upper lobe emphysema, the study subjects were treated for community-acquired upper lobe pneumonia [41]. After pneumonia treatment and resolution, the most diseased and hyperinflated lung area lost lobar volume and significant improvement in respiratory function was reported. The natural and interesting outcome of these individuals who did not undergo BLVR was similar to that of patients who developed CAO after BLVR.

Deaths

Mortality was reported in 0.0–3.5% of patients after the TR period and 0.0–11.1% of the subjects during the follow-up [14–24]. In these studies, mortality was not thought to be entirely dependent on coil procedures, and deaths due to non-procedural/non-respiratory causes such as hemorrhagic stroke, severe urinary sepsis, esophageal cancer can also be observed [19]. However,

the cause of mortality is usually severe pneumonia, COPD exacerbation, respiratory failure and sepsis [14, 19–23].

Hiccups

Hiccups are a very rare complication. It is likely caused by the proximity of the coils to the diaphragm or the uptake of the diaphragm owing to the reduction in lower lobe volume. The incidence rate was reported to be 1.6% in one study, and spontaneous recovery has been documented [14]. In stubborn cases, removal of the coil may be considered.

Discussion

Bronchoscopic lung volume reduction coil treatments are an option especially for patients with severe hyperinflation and emphysema who do not respond to medical/supportive treatments. BLVR coil treatments have been shown to improve functional and clinical parameters in many studies [14, 15, 17, 20–24]. In the RENEW study, which included a 1-year follow-up, partial improvement in 6-MWT and respiratory functions were reported in those who received coil therapy compared to usual care, and any complication has been reported in 34.8% of those treated with coil therapy and 19.1% in usual care [22]. In the REVOLENS study, which included a 2-year follow-up, FEV₁ and dyspnea score (modified Medical Research Council) were not statistically significant compared to the initial value, while the quality of life score (Saint George's Respiratory Questionnaire), 6-minute walk test and residual volume values remained statistically significant [21]. Twenty-six patients had 45 serious adverse events (SAEs) in the first year, while 27 SAEs in twenty patients were observed in the second year. As a respiratory complication, 1 lung nodule, 1 lung transplantation, 4 pneumonia and 12 cases of COPD exacerbation were reported, while unexpected SAEs and pneumothorax did not develop [21]. Considering the potential complications, great care must be taken in the selection of the patients for these treatments. In addition, some studies did not classify complications as a recover period (first 30 days) or follow-up (after > 31 days), which naturally leads to a lack of exact rates for complications (e.g. 0–75% for bleeding).

Various complications have been reported during and after BLVR coil treatments (Figure 1). Patients should be informed about the complications that may develop and their written informed consent must be obtained prior to the

procedure. Despite the observed complications, it can be said that this treatment is effective and safe considering the medium- to long-term outcomes [14–24]. The high COPD exacerbation rate in the studies suggests that the use of premedication, prophylactic antibiotics, and corticosteroids is warranted. Other observed complications have not proven to be preventable after premedication. In fact, some complications may be related to the experience of the endoscopist. In addition, we also recommend that patients should carefully monitor their current vaccination status (influenza and pneumococcal) because a large proportion of persons are at the COPD GOLD III or IV stage. We hypothesize that the incidence of some complications in vaccinated patients will be lower, although this hypothesis requires future testing.

Mortality rates in the follow-up period after BLVR coil therapy were reported to average at 3.9% (range 0.0–11.1%) [14–24]. A 3-year survival rate of 84% was found in the longest follow-up study of BLVR coil treatment [19]. All patients undergoing BLVR are at the COPD GOLD III and GOLD IV stages. Hence, these subjects already have a natural comorbidity. A 15-year survival rate of 7.3% (5.3% for GOLD III patients and 0.0% for GOLD IV patients) was found in all COPD groups in a recent study [42]. However, GOLD III and IV patients were also reported to have a life expectancy of 6.1 and 3.1 years, respectively, when hospitalized with exacerbation [42]. The situation is not different in individuals with emphysema. In a study of an emphysema patient group with a mean FEV₁ of 26.7 ± 7.0%, mortality was reported as 12.7 per 100 person-years over a mean follow-up of 3.9 years [43]. These results suggest that mortality rates with BLVR are likely lower than those in untreated patients with similar morbidity.

Patients with emphysema and GOLD IV COPD are potential or borderline candidates for lung transplantation. According to the guidelines of the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation (2014), persons with FEV₁ < 15–20% are considered candidates for lung transplantation [44]. However, when this value is < 25%, it is suggested that patients are included in the transplantation list [44]. In a published case report, bilateral BLVR coil therapy was applied to an end-stage emphysema patient enrolled in the lung transplantation list [45]. After treatment, the patient's FEV₁ increased from 19% to 21, and the RV decreased from 289% to 254%. Transplantation was postponed because of improvement

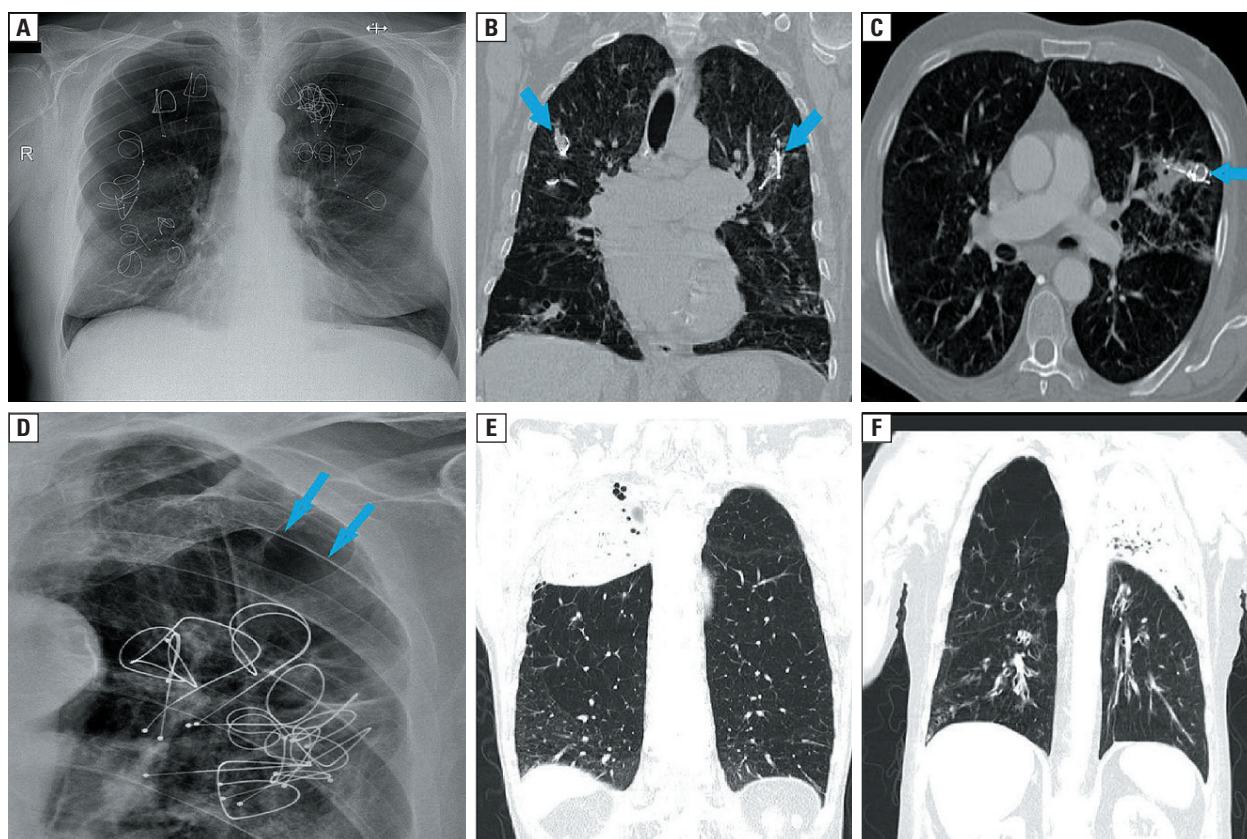


Figure 1. Successful bilateral endobronchial coil implantation (A), bilateral upper lobe coil-associated opacities (B), unilateral left upper lobe coil-associated opacities (C), left upper lobe coil implantation and pneumothorax (D), right upper lobe coil implantation and pneumonia (E), left upper lobe coil implantation and pneumonia (F)

in clinical symptoms and pulmonary function, and was performed after 3.5 years. In another study, BLVR coil treatments were found to be safe during the 12-month follow-up among transplant candidate patients with FEV₁ values below 25% [46]. This result is an example of how BLVR coil therapy can buy time for people awaiting lung transplantation.

Bacterial colonization in the airway is frequently observed in BLVR coil therapy patients and represents a significant opportunity for improved outcomes. In one study, colonization by *Pseudomonas* was reported in 8.1% of patients who were treated with BLVR coil treatment [14]. A separate 2017 study reported the detection of at least one potential pathogen in 47% of the BLVR coil patients. These pathogens, *Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa*, were detected in 9%, 6%, 6%, and < 5% of cases, respectively [47]. Therefore, it is important to perform sputum examination before the first procedure. Although there is no definite contraindication in patients with *Pseudomonas aeruginosa*

colonization, it should be kept in mind that this may be a relative contraindication if the patient has frequent exacerbations or uses antibiotics regularly. In a case report published by Casutt *et al.*, a patient who had previous *Pseudomonas* infection but had no growth in current sputum culture developed severe pneumonia after endobronchial coil treatment [48]. In the post-procedure sputum culture, *Aspergillus fumigatus* and *Pseudomonas aeruginosa* colonies were observed. Risk–benefit evaluation of BLVR treatments in patients who have previously had bacterial infection or colonization is recommended.

Medical devices manufactured from materials such as nickel-titanium alloy (nitinol) generally have an intrinsic antibacterial effect and resistance to bacterial formation [49]. However, *Acinetobacter*, *Alcaligenes*, *Pseudomonas*, *Comamonas*, *Stenotrophomonas*, and *Aspergillus* families can develop nickel resistance through plasmids and may contribute to CAO or pneumonia [50]. An example of this are the cases of *Aspergillus*-associated cavitation [29, 30]. It is thus clear that this issue requires further research.

Conclusions

Bronchoscopic lung volume reduction coil therapy is a minimally invasive nonsurgical procedure with potential complications in both the early and late follow-up periods. However, patients treated with BLVR have lower mortality rates than untreated patients with similar morbidity. Based on the findings of this review, we can estimate that premedication one day before and just before the procedure may reduce potential complications. Some medical centers apply and recommend 30-day macrolide treatment after the procedure. New generation SGD may be preferred to avoid complications due to endotracheal intubation. Moreover, further research is needed to identify risk factors, prevent potential complications, and a common consensus is required for routine preventive treatment.

Conflict of interest

The author has stated explicitly that there are no conflicts of interest in connection with this article.

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